

# Web-based Supplementary Materials for “Assessing Association for Bivariate Survival Data with Interval Sampling: A Copula Model Approach with Application to AIDS Study” by Hong Zhu and Mei-Cheng Wang

The following conditions are assumed throughout the paper.

- (1) Assume that standard regularity conditions for maximum likelihood estimate hold.
- (2) Define functions

$$W_{\alpha}\{\alpha, S_Y(y), S_Z(z)\} = \frac{\partial \log l(\alpha, u, v)}{\partial \alpha}, \quad V_{\alpha}\{\alpha, S_Y(y), S_Z(z)\} = \frac{\partial^2 \log l(\alpha, u, v)}{\partial \alpha^2}$$

$$V_{\alpha,1}\{\alpha, S_Y(y), S_Z(z)\} = \frac{\partial^2 \log l(\alpha, u, v)}{\partial \alpha \partial u}, \quad V_{\alpha,2}\{\alpha, S_Y(y), S_Z(z)\} = \frac{\partial^2 \log l(\alpha, u, v)}{\partial \alpha \partial v}$$

Assume that they are continuous and bounded for  $(y, z) \in \mathcal{A} = [y_-, y_+] \times [z_-, z_+]$ .

## Web Appendix: Proof of Theorem 1

Under the assumed conditions listed above, we derive the asymptotic properties of  $\hat{\alpha}(\theta)$ . For simplicity of discussion, we denote  $\hat{\alpha}(\theta)$  by  $\hat{\alpha}$  since  $\theta$  is known. First, we show the consistency of  $\hat{\alpha}$ . The score function of  $\alpha$  is  $U_{\alpha}^{(c)}(\alpha, S_Y, S_Z) = \frac{\partial}{\partial \alpha} \sum_{i=1}^n \log l(\alpha, S_Y, S_Z)$  and pseudo score function is  $U_{\alpha}^{(p)}(\alpha, \hat{S}_Y, \hat{S}_Z) = \frac{\partial}{\partial \alpha} \sum_{i=1}^n \log l(\alpha, \hat{S}_Y, \hat{S}_Z)$  by substituting  $S_Y(y, \theta)$  and  $S_Z(y, \theta)$  in score function by  $\hat{S}_Y$  and  $\hat{S}_Z$ . We have  $\hat{S}_Y(\cdot)$  converges in probability to  $S_Y(\cdot)$  uniformly in  $[y_-, y_+]$ ,  $\hat{S}_Z(\cdot)$  converges to  $S_Z(\cdot)$  uniformly in  $[z_-, z_+]$ , and  $U_{\alpha}^{(c)}(\alpha, u, v)$  is a continuous function of  $u$  and  $v$ . Therefore, for every  $\alpha$ ,  $U_{\alpha}^{(p)}(\alpha, \hat{S}_Y, \hat{S}_Z)$  converge to  $U_{\alpha}^{(c)}(\alpha, S_Y, S_Z)$  in probability. This

pointwise convergence implies that the solution to  $U_\alpha^{(p)}(\alpha, \hat{S}_Y, \hat{S}_Z)$ ,  $\hat{\alpha}$ , is consistent by the similar arguments to those in Samuelsen (1997).

Next, we show the asymptotic normality of  $\hat{\alpha}$ . By Taylor expansion on the pseudo score function  $U_\alpha^{(p)}(\alpha, \hat{S}_Y, \hat{S}_Z)$  around  $\alpha_0$ , rearranging and evaluating it at  $\alpha = \hat{\alpha}$ , we get

$$n^{1/2}(\hat{\alpha} - \alpha_0) \cong \frac{-U_\alpha^{(p)}\{\alpha_0, \hat{S}_Y(Y_i), \hat{S}_Z(X_i)\}/\sqrt{n}}{\sum_{i=1}^n V_\alpha\{\alpha_0, \hat{S}_Y(Y_i), \hat{S}_Z(X_i)\}/n}$$

Since  $\hat{S}_Y(\cdot)$  converges in probability to  $S_Y(\cdot)$  uniformly in  $[y_-, y_+]$ ,  $\hat{S}_Z(\cdot)$  converges to  $S_Z(\cdot)$  uniformly in  $[z_-, z_+]$ , and  $V_\alpha(\alpha, u, v)$  is a continuous function of  $u$  and  $v$ ,  $|V_\alpha\{\alpha_0, \hat{S}_Y(y), \hat{S}_Z(z)\} - V_\alpha\{\alpha_0, S_Y(y), S_Z(z)\}|$  converges in probability to zero for  $(y, z) \in \mathcal{A} = [y_-, y_+] \times [z_-, z_+]$ . Thus  $\sum_{i=1}^n -V_\alpha\{\alpha_0, \hat{S}_Y(Y_i), \hat{S}_Z(X_i)\}/n$  and  $\sum_{i=1}^n -V_\alpha\{\alpha_0, S_Y(Y_i), S_Z(X_i)\}/n$  are asymptotically equivalent, which by the law of large numbers converges to  $\rho_1^2$ , specified as

$$\rho_1^2 = E[-V_\alpha\{\alpha_0, S_Y(Y_i), S_Z(X_i)\}] = \int_{\mathcal{A}} -V_\alpha\{\alpha_0, S_Y(y), S_Z(z)\} dJ_{\alpha_0}(y, z, \delta)$$

where  $J_{\alpha_0}$  is the joint distribution of  $(Y, X, \delta)$ . Next, we have

$$\begin{aligned} n^{-1/2}U_\alpha^{(p)}(\alpha_0, \hat{S}_Y, \hat{S}_Z) &= n^{1/2} \int_{\mathcal{A}} W_\alpha\{\alpha_0, \hat{S}_Y(y), \hat{S}_Z(z)\} dJ_n(y, z, \delta) \\ &= n^{1/2} \int_{\mathcal{A}} W_\alpha\{\alpha_0, \hat{S}_Y(y), \hat{S}_Z(z)\} dJ_{\alpha_0}(y, z, \delta) \\ &+ n^{1/2} \int_{\mathcal{A}} W_\alpha\{\alpha_0, \hat{S}_Y(y), \hat{S}_Z(z)\} (dJ_n - dJ_{\alpha_0})(y, z, \delta) \\ &= \pi_n(\alpha_0, \hat{S}_Y, \hat{S}_Z) + \eta_n(\alpha_0, \hat{S}_Y, \hat{S}_Z) \end{aligned}$$

where  $J_n$  is the empirical distribution of  $J_{\alpha_0}$ . We further decompose  $\eta_n$  into two terms,

$$\begin{aligned} \eta_n(\alpha_0, \hat{S}_Y, \hat{S}_Z) &= n^{1/2} \int_{\mathcal{A}} [W_\alpha\{\alpha_0, \hat{S}_Y(y), \hat{S}_Z(z)\} - W_\alpha\{\alpha_0, S_Y(y), S_Z(z)\}] \\ &\quad (dJ_n - dJ_{\alpha_0})(y, z, \delta) \\ &+ n^{1/2} \int_{\mathcal{A}} W_\alpha\{\alpha_0, S_Y(y), S_Z(z)\} (dJ_n - dJ_{\alpha_0})(y, z, \delta) \end{aligned}$$

Because  $\hat{S}_Y \rightarrow S_Y$ ,  $\hat{S}_Z \rightarrow S_Z$ ,  $n^{1/2}(J_n - J) \rightarrow O_p(1)$ , and  $W_\alpha$  is continuous and bounded, by the dominated convergence theorem, the first term in  $\eta_n$  convergence to 0. The second term of  $\eta_n$  is a sum of  $n$  i.i.d. random variables

of mean zero and variance  $\rho_1^2$ , so it converges to normal with mean zero and variance  $\rho_1^2$  by the central limit theorem. Using Von Mises expansion on  $\pi_n(\alpha_0, \hat{S}_Y, \hat{S}_Z)$  around  $S_Y$  and  $S_Z$ , we get

$$\begin{aligned}\pi_n(\alpha_0, \hat{S}_Y, \hat{S}_Z) &\cong \pi_n(\alpha_0, S_Y, S_Z) + n^{1/2} \int IC_Y(y) d(\hat{S}_Y - S_Y)(y) \\ &+ n^{1/2} \int IC_Z(z) d(\hat{S}_Z - S_Z)(z) \\ &= 0 + n^{1/2} \int IC_Y(y) d(\hat{S}_Y - S_Y)(y) \\ &+ n^{1/2} \int IC_Z(z) d(\hat{S}_Z - S_Z)(z)\end{aligned}$$

where  $IC_Y$  and  $IC_Z$  are obtained by differentiating  $\pi\{\alpha_0, (1 - \varepsilon_1)S_Y + \varepsilon_1\hat{S}_Y, (1 - \varepsilon_2)S_Z + \varepsilon_2\hat{S}_Z\}$  with respect to  $\varepsilon_1$  and  $\varepsilon_2$  and evaluating at  $\varepsilon_1 = \varepsilon_2 = 0$ , and  $IC_Y(y) = -\int_0^y \int_0^{z_0} V_{\alpha,1}\{\alpha_0, S_Y(u), S_Z(z)\} j_{\alpha_0}(u, z, \delta) dz du$  and  $IC_Z(z) = -\int_0^z \int_0^{y_0} V_{\alpha,2}\{\alpha_0, S_Y(y), S_Z(u)\} j_{\alpha_0}(y, u, \delta) dy du$ . By the counting process asymptotic techniques,  $n^{1/2}\{\hat{S}_Y(y) - S_Y(y)\}$  is asymptotically equivalent to a sum of  $n$  i.i.d. random variables as  $\sum_i n^{-1/2} I_1^0(Y_i)(y)$ , and  $n^{1/2}\{\hat{S}_Z(z) - S_Z(z)\}$  is asymptotically equivalent to a sum of  $n$  i.i.d. random variables as  $\sum_i n^{-1/2} I_2^0(X_i, \delta_i)(z)$ .  $I_1^0$  and  $I_2^0$  are martingales, defined as  $I_1^0(Y_i)(y) = -S_Y(y) \{ \int_0^y \frac{dN_{1i}(u)}{p(Y \geq u)} - \int_0^y \frac{I(Y_i \geq u) d\Lambda_1(u)}{p(Y \geq u)} \}$  and  $I_2^0(X_i, \delta_i)(z) = -S_Z(z) \{ \int_0^z \frac{dN_{2i}(u)}{p(Z \geq u, C_2 \geq u)} - \int_0^z \frac{I(X_i \geq u) d\Lambda_2(u)}{p(Z \geq u, C_2 \geq u)} \}$  where  $C_2 = C - T - Y$ ,  $N_{1i}(u) = I(Y_i \leq u)$ ,  $N_{2i}(u) = I(Z_i \leq u, \delta_i = 1)$ , and  $\Lambda_1$  and  $\Lambda_2$  are the cumulative hazard functions for  $Y$  and  $Z$ . Then we have

$$\begin{aligned}\pi_n(\alpha_0, \hat{S}_Y, \hat{S}_Z) &\cong n^{-1/2} \left[ \sum_i \int_{\mathcal{A}} V_{\alpha,1}\{\alpha_0, S_Y(y), S_Z(z)\} I_1^0(Y_i)(y) dJ_{\alpha_0}(y, z, \delta) \right. \\ &+ \left. \int_{\mathcal{A}} V_{\alpha,2}\{\alpha_0, S_Y(y), S_Z(z)\} I_2^0(X_i, \delta_i)(z) dJ_{\alpha_0}(y, z, \delta) \right] \\ &= n^{-1/2} \left\{ \sum_i I_1(Y_i, \alpha_0) + I_2(X_i, \delta_i, \alpha_0) \right\}\end{aligned}$$

which is a sum of  $n$  i.i.d. random variables. Since  $IC_Y$  and  $IC_Z$  are deterministic functions, the expectations of  $I_1$  and  $I_2$  are 0. By the central limit theorem,  $\pi_n(\alpha_0, \hat{S}_Y, \hat{S}_Z)$  converges to normal with mean 0 and variance  $\rho_2^2$ , specified as

$$\rho_2^2 = E[\{I_1(Y, \alpha_0) + I_2(X, \delta, \alpha_0)\}^2] = \int_{\mathcal{A}} \{I_1(y, \alpha_0) + I_2(z, \delta, \alpha_0)\}^2 dJ_{\alpha_0}(y, z, \delta)$$

Note that we have proved that  $\pi_n(\alpha_0, \hat{S}_Y, \hat{S}_Z)$  is asymptotically equivalent to  $n^{1/2}\{\sum_i I_1(Y_i, \alpha_0) + I_2(X_i, \delta_i, \alpha_0)\}$ , and  $\eta_n(\alpha_0, \hat{S}_Y, \hat{S}_Z)$  is asymptotically

equivalent to  $n^{1/2} \sum_i W_\alpha \{\alpha_0, S_Y(Y_i), S_Z(X_i)\}$ . Since  $\pi_n$  and  $\eta_n$  are asymptotically independent by the similar arguments in the proof of Theorem 1 in Shih and Louis (1995),  $n^{1/2}(\hat{\alpha} - \alpha_0)$  converges to normal with mean zero and variance  $\sigma^2 = (\rho_1^2 + \rho_2^2)/\rho_1^4$ .

The variance estimator  $\hat{\sigma}^2$  can be obtained by replacing  $J$  by its empirical distribution function  $J_n$ , and  $S_Y, S_Z, \alpha$  by  $\hat{S}_Y, \hat{S}_Z, \hat{\alpha}$ . Specifically,

$$\begin{aligned} \hat{\rho}_1^2 &= \int_{\mathcal{A}} -V_\alpha \{\alpha_0, S_Y(y), S_Z(z)\} dJ_n(y, z, \delta) = \frac{1}{n} \sum_{i=1}^n -V_\alpha \{\hat{\alpha}, \hat{S}_Y(Y_i), \hat{S}_Z(X_i)\}. \\ \hat{\rho}_2^2 &= \int_{\mathcal{A}} \{\hat{I}_1(y, \hat{\alpha}) + \hat{I}_2(z, \delta, \hat{\alpha})\}^2 dJ_n(y, z, \delta) = \frac{1}{n} \sum_{i=1}^n \{\hat{I}_1(Y_i, \hat{\alpha}) + \hat{I}_2(X_i, \delta_i, \hat{\alpha})\}^2 \\ &= \frac{1}{n} \sum_{i=1}^n \left[ \frac{1}{n} \sum_{j=1}^n V_{\alpha,1} \{\hat{\alpha}, \hat{S}_Y(Y_j), \hat{S}_Z(X_j)\} \hat{I}_1^0(Y_i)(Y_j) \right. \\ &\quad \left. + \frac{1}{n} \sum_{j=1}^n V_{\alpha,2} \{\hat{\alpha}, \hat{S}_Y(Y_j), \hat{S}_Z(X_j)\} \hat{I}_2^0(X_i, \delta_i)(X_j) \right]^2 \end{aligned}$$

where  $\hat{I}_1^0(Y_i)(Y_j)$  and  $\hat{I}_2^0(X_i, \delta_i)(X_j)$  are the corresponding empirical estimators. Since  $\hat{\alpha} \rightarrow \alpha_0$ ,  $\hat{S}_Y \rightarrow S_Y$ ,  $\hat{S}_Z \rightarrow S_Z$ , and  $V_\alpha, V_{\alpha,1}, V_{\alpha,2}$  are continuous functions,  $\hat{\rho}_1^2$  converges to  $\rho_1^2$ ,  $\hat{\rho}_2^2$  converges to  $\rho_2^2$ , and  $\hat{\sigma}^2$  converges to  $\sigma^2$  in probability respectively.

## References

- [1] Samuelsen, S. O. (1997). A pseudolikelihood approach to analysis of nested case-control studies. *Biometrika* **84**, 379–394.
- [2] Shih, J. H. and Louis, T. A. (1995). Inferences on the association parameters in copula models for bivariate survival data. *Biometrics* **51**, 1384–1399.